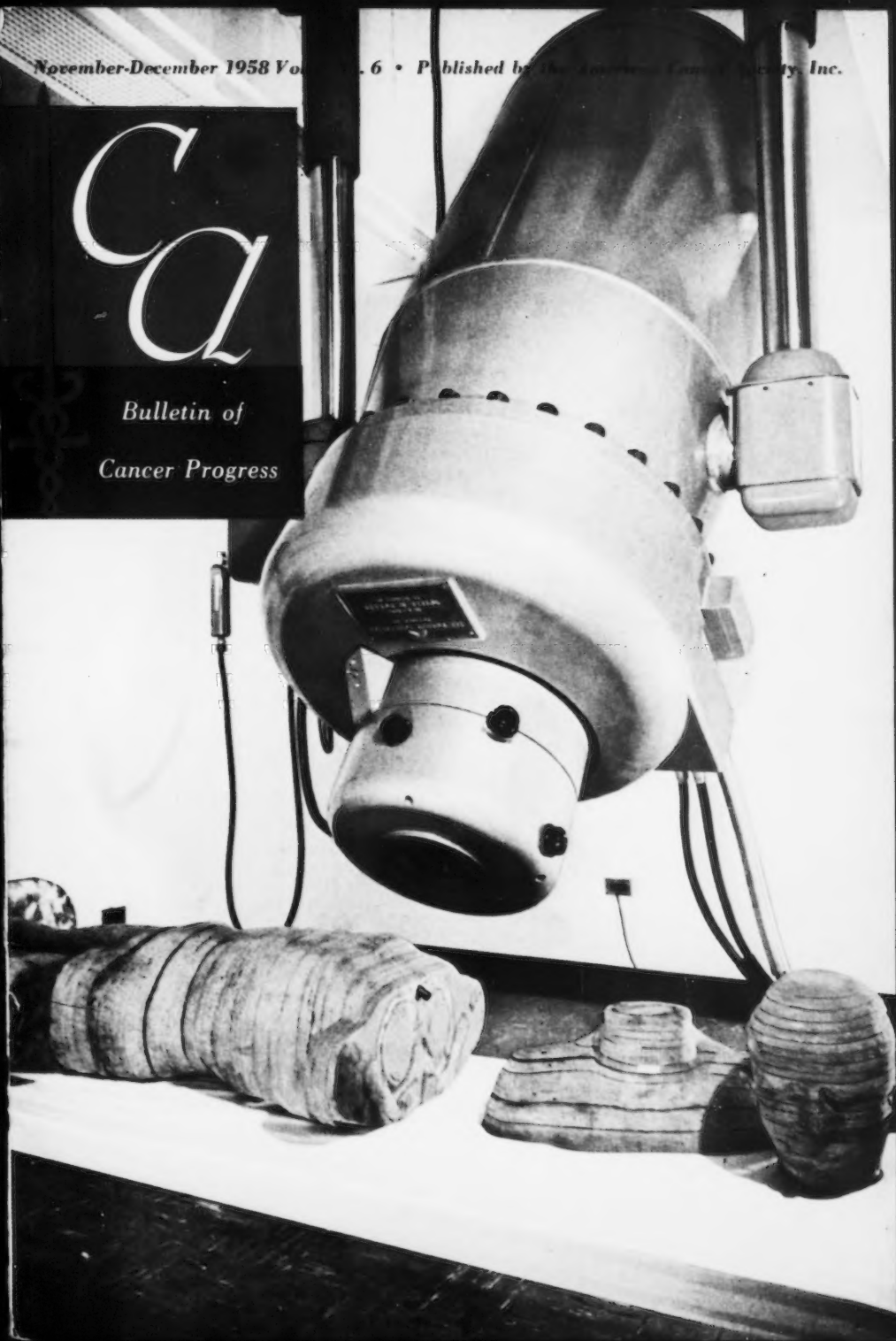


November-December 1958 Volume 6 • Published by the American Cancer Society, Inc.

Ca

*Bulletin of  
Cancer Progress*



*progress  
is being  
made*

Despite the continuing increase in cancer deaths, substantial progress is being made in the control of this disease. In fact, the increase in cancer deaths is due largely to the increasing age of the population which brings more persons into the age groups in which cancer takes its greatest toll.

Advances in cancer control have been made on all fronts. An increasing proportion of the population is informed about cancer and is seeking medical advice earlier than ever before. Practicing physicians are more interested in cancer and are better prepared to deal with it effectively. More and more specially trained minds are being applied to research in all the sciences related to cancer. Increasing cooperation among these groups and rapidly increasing financial support are greatly accelerating progress toward the eventual cure or ultimate prevention of this disease.

Surgery is saving the lives of many cancer patients; yet surgery has reached a stage of perfection that precludes any

great increase in life salvage from that source. Likewise, the comparatively new science of radiology, with its supervoltage X-ray machines and its isotopes, can scarcely be expected to develop into a much more potent therapeutic modality.

The ultimate conquest of cancer will have to await research achievements that will provide definitive measures of prevention or cure. On the other hand, early diagnosis and the utilization of effective forms of treatment currently available hold real potentialities for further reduction of the cancer death rate.

The family physician is in a position to contribute most to this reduction. Routine, systematic physical examinations, utilizing all the modern techniques of cancer detection, could disclose significant numbers of precancerous lesions as well as cancers in an early curable stage. Discontinuance of cigarette smoking could eventually reduce the incidence of lung cancer by as much as 90 per cent.

Until the research laboratories supply a preventive or cure, hope for saving lives from cancer rests primarily with the family physician and his informed and cooperating patients.

*D. S. Siegel*

Senior Vice President for Research  
and Medical Affairs and Deputy  
Executive Vice President,  
American Cancer Society, Inc.

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**Cover**—The two-million-volt Van de Graaff X-ray generator in the Radiation Therapy Department of Memorial Center for Cancer and Allied Diseases, New York, N. Y.

The 2-million-volt Van de Graaff X-ray generator is the thirteenth newly developed model now installed in treatment centers throughout the United States. It was formally presented to the Center by the Donner Foundation at dedication ceremonies September 23, 1958. Compared with conventional X rays, supervoltage

radiations possess clinically advantageous properties arising from their greater penetration into tissue, permitting delivery of a large dose of radiation to a deep-seated tumor, with relatively small doses to adjacent structures and to the skin. With data from the physicist's irradiation of tissue equivalent substances, such as the sectioned presdwood-cork-bone phantom shown, it is now possible to estimate more accurately the energy distribution throughout the body when a cancerocidal dose is delivered.

# NEWSLETTER

NOVEMBER-DECEMBER, 1958

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The Seventh International Cancer Congress in London produced many interesting research minutiae but nothing of major consequence so far as cancer control goes. A careful review of the abstracts and published accounts of the meeting offers no substance to support the recurring suggestions that a "breakthrough" in cancer may be at hand. Generally the papers followed faithfully the conventional fashions in cancer research.

Kreyberg (Oslo): Lung cancer patients can be divided, morphologically and clinically, into two groups: (1) Squamous, large and oat cell carcinomas related to external irritants (nickel, chromium, asbestos, radon, smoking and possibly coal tar fumes); and (2) adenocarcinoma, bronchiolar, adenoma and salivary gland tumors apparently not related to irritants.

Farber (Boston): "Two of the most important and promising" directions of chemotherapy research are the anti-metabolites (folic acid and purine antagonists) and the antibiotics (the actinomycins C and D).

Larionov (Moscow): A number of sarcolysine peptides produce regression in certain transplanted tumors without depressing hematopoiesis.

Kirkman (San Francisco): In the Syrian hamster kidney tumor, testosterone propionate may (1) act as a non-specific carcinogen, (2) play a role in its transition from hormone dependence to autonomy or (3) act as a synergist.

Bielschowsky (Dunedin, N. Z.): Goitrogen stimulation makes thyroid tumors become functional and take up  $I^{131}$ . Thyroxin suppresses TSH secretion and leads to involution of pituitary-dependent tumors.

Furth et al. (Boston): Mice exposed to atomic bomb radiation developed enormous, autonomous and functional pituitary tumors, most of them secreting ACTH but others producing TSH. Pituitary irradiation changes specific cells in the pituitary mosaic, disturbing the homeostatic mechanism and causing tumors either in the pituitary or hyperstimulated target organ.

Sachs (Rehovoth, Israel): With homotransplantation, tumors gain antigenicity. But, probably due to extra- or intracellular neutralization by antigens of tumor cells

and the host's cytotoxic factors, there is observed a definitely increased resistance to the immune response.

Weinhouse (Philadelphia): The high glycolytic activity of tumors may be due to the cell membrane's extraordinary permeability to glucose. These studies show no respiratory impairment in tumors -- no enzymatic defects in carbon or electron transport or associated phosphorylation. Fatty acids are the principal source of endogenous respiration, largely replaced by glucose when present.

Heidelberger (Madison): Carcinogenic hydrocarbon derivatives have been traced and found to bind, at their K region, with skin proteins.

Kavetsky (Kiev): Disturbance of the rhythm of pituitary gonadotropic and mammatropic activities is an outstanding feature of high breast tumor strain mice. Pituitary activity is controlled by the nervous system. Neuroses alter nerve and pituitary and induce more and earlier breast tumors.

R. M. Graham (Buffalo): Vaginal smear screening of an entire population may yield as many as 7 per thousand positives -- and in asymptomatic women, as low as 3 per thousand. To screen most effectively, one should consider the fact that certain races and women married before 20 have more than average susceptibility.

Ackerman and Spjut (St. Louis): In patients with lung cancer (proved later), sputum tests were positive in 60 per cent -- in 80 per cent for those undergoing three or more tests and in 90 per cent for those with epidermoid cancer. The test was positive in 59 patients who did not yield a positive bronchoscopic biopsy. There were no false positives. Exfoliative cytologic examination is advisable both before lung operation and, for prognosis, after.

Lopes Cardozo (Leiden): Use the aspiration cytologic method at the first visit in each unexplained lump provided it does not pulsate and is not reducible. Still neglected but diagnostically superior to biopsy is needle aspiration of lumps in lymph nodes, retromandibular region, breast, thyroid, testis, muscle, subcutaneous tissues, skeleton, enlarged liver, spleen and sometimes the renal region.

Haagensen (New York): Breast cancer surgery is being discredited because of indiscriminate radical mastectomy in all stages of cancer and poor techniques. Careful selection excludes 50 per cent of the patients who have no

(Continued after page 216)



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TOPIC: CANCER PROGRESS

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ARTICLES IN *CA* ARE INDEXED IN CURRENT LIST OF MEDICAL LITERATURE AND QUARTERLY CUMULATIVE INDEX MEDICUS, AND SOME ARE ABSTRACTED IN CHEMICAL ABSTRACTS, BIOLOGICAL ABSTRACTS, EXCERPTA MEDICA AND ABSTRACTS OF WORLD MEDICINE.

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# Progress in Surgery of Cancer

*Warren H. Cole, M.D.*

Much progress has been made in the surgery of cancer during the past 15 years. This improvement has been made possible by more accurate utilization of blood replacement, better knowledge of surgical physiology (including pre- and postoperative care), greater improvement in anesthesia and an extension of the limits of the operation. It is surprising that it took us so long to appreciate the value of adequate blood replacement during a major operative procedure. The extension of the resected tissue along with the tumor has been made possible only by the three preceding mechanisms. The first three improvements mentioned above have resulted in a marked lowering of the operative mortality rate, and extension of the operation has resulted in a higher five-year survival rate. However, we can scarcely expect increased progress in these two directions, but a better knowledge of surgical physiology will enable us to improve the patient's ability to withstand the operation, thus reducing the operative mortality rate. We can expect no improvement from an increase in the amount of resected tissue, since, in general, a greater extension than now practiced would involve removal of vital tissue.

## **Delay Between Onset of Symptoms and Definitive Therapy**

At the present time surgery and radiology are the only two methods of treatment for the cure of cancer. Since neither of them is very effective in the treatment of late cancer, we must exert all possible effort to eliminate delay in therapy. Unfortunately both the patient and the physician are responsible for this delay. It is

perhaps not fully realized that many, and in fact most, tumors including carcinoma of the stomach, colon, etc., have already developed to a sizable lesion by the time they begin to produce symptoms. Accordingly if a patient has dyspepsia or symptoms of that type longer than two or three weeks, he should have a thorough examination for cancer of the intra-abdominal organs. Since X-ray examination, including the use of barium, is very accurate in detecting cancer of the intestinal tract it is obviously desirable to obtain this type of examination if there is a possibility that cancer is present. Frequent use of X rays for this purpose will, of course, result in numerous negative examinations. However, it is better to have numerous negative examinations than to detect a tumor too late for possibility of a cure. When a gastric ulcer is discovered by X ray, nonsurgical treatment is often carried out too long, particularly since 12 to 15 per cent of gastric ulcers are malignant, and since their removal is associated with a much higher five-year survival rate than in patients with gastric cancer of the proliferative type.

It must be emphasized that the first operation for cancer represents the one most likely to effect a cure. If recurrence develops because of failure to remove the entire cancer or because of implantation of cancer in the wound, the effect of therapy is diminished sharply. However, removal of a recurrent cancer is often curative, especially if it is of the implanted type.

## **The Great Value of Biopsy**

Biopsy properly employed is very helpful in increasing curability of cancer, and allows us to carry out definitive therapy in

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the earlier stages of the disease. Wherever possible definitive surgery should be carried out at the same operation during which a biopsy is performed. This minimizes the danger of spread of the disease. A frozen section can be obtained at the time of operation and reported to the surgeon within a few minutes, thus allowing the two procedures to be followed at the same operation. I wish to emphasize, however, that the biopsy must be done properly. After the biopsy specimen is obtained and a positive result reported, the instruments, gloves, drapes, etc., must be changed to eliminate the possibility of dissemination by the surgeon. Wherever possible the biopsy should be excisional in type. For example, when a nodule is encountered in the breast the entire nodule should be removed with a wide area of normal breast tissue adjacent to it. If the mass is so big that it cannot be removed in toto without sacrificing the entire breast, it is usually better to remove the entire breast if there is a strong possibility that the mass is malignant.

The importance of the method in performing a biopsy is emphasized by data reported by Davis,<sup>5</sup> who studied the five-year survival rates in more than 700 patients observed in the Tumor Clinic and the University of Illinois Hospitals. In many of these patients the biopsy was performed outside the hospital and the patient sent in to us for definitive care. In this group of patients more than 24 hours elapsed from the time of biopsy to the time of radical resection. In 27 patients having aspiration biopsy the five-year survival rate was only 19 per cent; in 39 patients having incisional biopsy the five-year survival rate was only 5 per cent, whereas in 29 patients having excisional biopsy the five-year survival rate was 72 per cent. This is a small series of patients but the difference between the first two types of biopsy and the third type is so striking that one is forced to conclude that the method of obtaining the biopsy specimen is important. Unfortunately we are not always able to do an excisional biopsy for all types of tumors. This is particularly true in carcinoma of the rectum,

esophagus and many other organs where biopsy is routinely practiced. However, when the biopsy specimen is taken from a mucosal surface it is doubtful that the associated trauma affects the results significantly.

### Dissemination of Cancer

Although there is not much probability of obtaining better five-year survival rates through the four mechanisms previously mentioned, there is good evidence for expecting better survival rates if we utilize procedures designed to prevent the dissemination of cancer.

We must emphasize that during examination of tumors that might be malignant manipulation must be carried out very gently. Likewise at operation the tumor must be handled very gently. If the mass itself is covered with gauze pads or some such material during its removal, the possibility of spread from the tumor may be minimized sharply. When the patient's skin is prepared for operation the mass should not be manipulated. This means that soap and water preparation is contraindicated in patients with palpable masses that might be malignant. The need for meticulous care in performing a biopsy has already been mentioned. In general, local anesthesia is undesirable in the treatment of patients with cancer because tumor cells may be forced into channels outside the area of excision.

All surgeons have seen patients in whom local recurrences develop because of implantation. Frequently it is impossible to determine the mechanism of development of the local recurrence. The possibility of implantation of tumors of the colon in the suture line at the time of resection has been emphasized by several authors.<sup>2, 7, 9, 11, 13</sup> Numerous mechanisms including irrigation of the lumen of the bowel, ligation of the lumen of the colon, ligation of vascular trunks leading to and from the tumor and irrigation of wounds with chemicals injurious to cancer cells (such as cloropactin) have been advised in efforts to minimize implantation. The danger of spreading cancer cells throughout

the wound by carrying the dissection too near the tumor, or failing to protect the wound edges, or failing to change gloves, instruments and drapes after contamination must be fully appreciated.

### **Venous Emboli**

Studies carried out by numerous workers<sup>1,8</sup> indicate that veins within the tumor may become invaded by the neoplasm. Workers at the University of Illinois<sup>3</sup> reported in 1954 finding cancer cells in veins draining from the tumor. More recently several authors<sup>6,10,12</sup> have reported finding cancer cells in the systemic venous system as well as in the veins draining the tumors. The exact significance of these cells is not known. We must assume that their presence is highly undesirable since the lethal factor in most tumors (except tumors of the oral cavity and neck) is dissemination by way of the venous system.

*Prophylactic Chemotherapy.* The use of anticancer agents at the time of curative operations for cancer has recently been suggested,<sup>4</sup> but insufficient time has elapsed to determine its value.

### **Prophylactic Surgery**

Numerous operations are performed primarily to prevent the development of cancer. The excision of carcinoma in situ of the cervix is an example of prophylactic surgery. The excision of certain nevi will prevent the possible development of a melanoma. It is well known that leukoplakia is a precancerous lesion; excision of this tissue will prevent the development of cancer. Polyps of the intestinal tract including the colon, rectum and stomach are precancerous lesions, and their excision prevents the development of cancer in that area. When granulation tissue is allowed to exist for many years following burns or other such injuries there is a great tendency for development of cancer. Such areas should be obliterated by skin grafts with or without excision of the granulating surface. One of the reasons for performing cholecystectomy,

which is one of our most common major operations, is to prevent carcinoma of the gallbladder.

### **Palliative Versus Curative Operations**

By the time the operation is performed the tumor has often invaded beyond the limits of curability. However, on many occasions there are strong indications to resect the tumor even though we know cure is not possible. These indications are particularly strong in carcinoma of the stomach, colon and rectum where the tumor is ulcerated and responsible for the loss of a large amount of blood and plasma. By resecting the ulcerating lesion the patient's malnutrition and anemia are often corrected very effectively at least for a few months, but we must remember that if a palliative resection is associated with a high mortality rate, it may not be indicated.

*Five-Year Survival.* Recent studies of five-year survivals reveal the fact that one or two tumors in the body are rarely cured even though resection of the curative type is performed. The most dramatic of these is carcinoma of the pancreas. Clinical observation now reveals that less than 5 per cent of patients operated on for carcinoma of the pancreas survive longer than five years. However, we must not confuse carcinoma of the ampulla of Vater with carcinoma of the pancreas since the five-year survival of patients with the former lesion is in the neighborhood of 25 per cent or even higher. It is now evident that carcinoma of the upper and middle third of the esophagus is associated with an unusually low five-year survival rate. Accordingly there is a tendency to change the type of operation in lesions of these two locations to a less formidable one to avoid the untenable situation of performing an operation with an extremely high mortality rate and extremely low five-year survival rate.

### **Rehabilitation**

The surgeon must always keep in mind the fact that the patient must live with the after-effects of his operation. Fre-

quently the resection must be extensive and followed by such marked disability that the patient's life may be so miserable he would prefer to die. There is, of course, no categorical solution to this problem since patients will not respond the same way to the various types of operations and deformities resulting from them.

Actually rehabilitation must start before the operation. The operation and its effects must be explained thoroughly to the patient. It is particularly important to explain the operation to patients who will have a colostomy. Often it will be necessary to allow the patient to talk to someone with a colostomy before he will consent to the operation. Hospital surroundings must be pleasant and the patient must be treated with tender care.

Of the various types of operations for carcinoma, radical neck operations requiring resection of the jaw and part of the cheek will be one of the most common types with a severe defect. Not only is the

deformity produced by this operation very unsightly, but also it often makes it impossible for the patient to swallow food. Life can, of course, be maintained effectively with a soft plastic tube through the nasal cavity into the stomach but this is not a desirable situation for permanent care. With proper cooperation between the surgeon and the plastic surgeon these defects can often be corrected at the time of operation by sliding a flap into the proper position. On some occasions fitting of an oral prosthesis may improve the patient's morale tremendously and allow him to eat reasonably solid food, and thus maintain proper nutrition more readily.

When amputations are performed it is desirable to fit the patient with a prosthesis as soon as possible to prevent him from becoming discouraged. If the patient loses his desire to resume activity it will be very difficult to teach him how to use prosthesis effectively and to return him to useful citizenship.

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Would you realize what Progress is, call it Tomorrow.—Victor Hugo

# Progress in Cancer Detection

## I. Rationale, Methods and Selection of Patients

*Walter E. O'Donnell, M.D., Louis Venet, M.D., and Emerson Day, M.D.*

The diagnosis of cancer in the patient who has developed suggestive symptoms or signs does not usually present a major problem to the alert, competent and thorough practitioner. Once suspicion of this diagnosis has been created, both physician and patient are sufficiently motivated to invest the time, expense and thoughtful attention required to rule the diagnosis in or out. There are, of course, special situations involving—singly or in combination—an uncooperative patient, an overworked physician, certain characteristically occult neoplasms or a lesion with highly atypical presenting symptoms or signs. Then the diagnosis may be long delayed or missed entirely. However, presently available methods of investigation, including X ray, biopsy, cytology, blood studies and other laboratory aids, suffice to bring home the diagnosis in about nine out of ten of those cases in which a major suspicion of cancer exists.

Establishing the diagnosis, however, is not enough. To be of benefit to the individual patient and to advance the overall cause of effective cancer control, diagnosis must be accomplished while the disease is still localized and susceptible to cure by surgery or radiotherapy. Once the so-called classical symptoms or signs of cancer have become manifest, the chance of cure usually falls off drastically. From this impression, bolstered by countless papers relating predicted curability and survival rates to size of lesion, presence or absence of symptoms, etc., stems the precept that "early diagnosis equals good prognosis" and all its natural corollaries.

Acknowledgments: Anne Ellis, Department of Preventive Medicine, Ralph E. Hertz, M.D., Rectum and Colon Service, the staffs of the Strang Cancer Prevention Clinic, and the Department of Preventive Medicine, Sloan-Kettering Institute and Memorial Hospital, New York, N. Y.

This thesis has its detractors who have been particularly vocal in recent years, but majority opinion still favors it.

Recognizing the imperative need for increasing the proportion of cancers found in their early stages, attention has turned in the last decade to the asymptomatic, presumably healthy adult. Efforts have been directed toward developing techniques by which a relatively standard clinical and laboratory examination of the well adult would identify those persons harboring silent—and presumably "early" and curable—cancers. This is true cancer detection. The vital role of the individual physician, heeding and investigating even the most minimal of symptoms, and performing at periodic intervals a routine complete physical examination with special reference to key sites, has been epitomized in the slogan "every doctor's office a cancer detection center." The fundamentals of this examination have been outlined in previous papers and will not be dealt with specifically.<sup>21</sup>

Reviewed here are the various cancer detection methods which have been proposed and their effectiveness in office examinations. Some methods have been tried and found wanting; others are in the process of evaluation. Still others have little to recommend them at present, but their introduction has been attended by such widespread interest and publicity as to warrant the physician's familiarity with them. Finally there is that group of procedures which seems well suited for inclusion in programs of cancer detection.

The ideal cancer detection method should have the following characteristics:

1. **SIMPLICITY.** The procedure should be an uncomplicated one, easily and quickly carried out, with a minimum of discomfort to the patient. It should be



adaptable for screening large numbers of patients.

2. **LOW COST.** It should be inexpensive in terms of equipment required and professional and technical time consumed.

3. **RELIABILITY.** The percentage of false positives must be kept to a minimum.

4. **SENSITIVITY.** The percentage of false negatives must also be low. Furthermore, the procedure must be capable of detecting disease in its early, localized stages.

5. **PRODUCTIVITY.** As a rule, the yield of cancer is a reflection of the incidence of the disease rather than the procedure itself.

It is immediately apparent that these criteria are not absolute but relative; not only that, but they are interdependent. For example, proctosigmoidoscopy is not exactly a "simple" procedure. However, what it lacks in simplicity it more than makes up in reliability and productivity. On the other hand, whatever virtues screening or detection methods for bone tumors, pheochromocytomas, etc., might have in terms of simplicity, reliability, sensitivity, etc., are cancelled out by the very low yield to be expected. The final assessment of the value of a cancer detection method lies in a critical evaluation of how many of these criteria it satisfies and to what degree.

One other aspect of the problem deserves consideration and that is the selection of patients for periodic cancer detection examinations. It is manifestly impossible to screen the entire population—not to mention making provision for this on a periodic basis. This problem is resolved by the identification of relatively high-risk individuals. The screening examination itself then narrows the field much further, and finally one is left with a group of cancer suspects.

The selective factors which determine the candidates for examination are many and varied. The most widely used and practical selective factor is that of age.

For maximum cancer yield, a relatively high age limit may be established such as 45 for women and 50 for men.<sup>6</sup> However, such an age for women is unrealistic in reference to cancers of the cervix and breast, whose incidence is significant after age 30. The final decision with regard to age minima is determined by the specific objectives of a given program and the demand in relation to available facilities.

In addition to age, practical selective factors have been established for certain types of cancer by epidemiologic investigations. Attention will be paid in succeeding paragraphs to this aspect of cancer-screening programs as they aid in determining who should be examined and what the cancer yield will be.

## GENERAL CANCER TESTS

The desire for a general cancer detection test which would screen large population groups is an obvious and natural one, but it seems no closer to fulfillment today than when the quest began in earnest over a quarter of a century ago. The advantages of a relatively simple, reliable and universally applicable laboratory divining rod for cancer similar to the serologic test for syphilis require little amplification.

Numerous tests have been proposed to exploit and measure some alleged characteristic of the cancer patient's blood, urine, body secretions or immunologic or enzyme systems. Thus far all the tests have foundered for the following reasons:

1. They have tended to assume that cancer is a single disease, with one or more constitutional common denominators which can be identified and used to form the basis for a general cancer test. Current knowledge suggests that this hypothesis may be unduly naive. The thesis that cancer is made up of a group of diseases of remarkably diverse etiology and behavior, sharing only certain cellular and pathological characteristics, has yet to be disproved.

2. They have also assumed that the alleged common denominator has two

further characteristics: (a) That it is a direct result of the cancer process per se, and not merely a reflection of non-specific body abnormalities secondary to the tissue destruction, body wasting, etc., associated with malignant diseases, (b) That it is present in the early, localized and potentially curable cancer.

Many cancer tests have been discredited or shown to be of no practical value because these assumptions have proved to be unwarranted.

3. Even if cancer tests have met the challenge of the first two items, they have been found without exception to be of no practical use in screening programs because of their unreliability. The percentage of false positives and false negatives has been too high to warrant clinical application of the technique.

In 1950 Homburger published an extensive review of the 60 such cancer diagnostic tests which had been proposed since 1930; a more recent publication by the same author has further expanded the list. Since that time others have been advanced but have not found practical application. Southam's observations regarding the possible role of cellular and humoral defense mechanisms in determining response to cancer homotransplantation may conceivably point the way to a fundamental reorientation of thinking and lead to means of evaluating these characteristics in patients.<sup>28</sup> The United States Public Health Service has published a monograph on the evaluation of cancer diagnostic tests which contains much useful information on this subject.<sup>7</sup>

The search for such a cancer test continues and may yield important information about certain fundamental characteristics of the cancer process, but the day when one of these techniques will simplify the task of finding early cancer seems far off indeed.

In the absence of a single reliable screening test, effective cancer detection depends upon thorough examination of individual patients for the first signs of disease utilizing established clinical meth-

ods. In large part, these lend themselves to incorporation into the type of systematized examination which is practical in the doctor's office. It should be mentioned that many presumably healthy adults will prove to have minimal symptoms which they do not regard as significant. The routine examination of these apparently well individuals serves to bring them to medical attention weeks or months before they would otherwise have sought it.

## HEAD AND NECK

Grouped under this anatomic heading by reason of convenience and proximity are such important cancer sites as the oral cavity, pharynx, larynx and thyroid as well as the skin of this region.

### The Problem

1956 Incidence (U.S.): 19,550\*—  
4.6% of cancer incidence.

1956 Mortality: 8749\*—  
3.5% of cancer mortality.

Male:female ratio is 3.5:1.

\*Excluding skin cancer.

### Selective Factors

Certain features which characterize the high-risk group are available from epidemiologic evidence.

1. **SMOKING HISTORY:** The smoking history of a patient can be of great assistance in screening for cancer in the oral cavity and larynx of asymptomatic individuals. *The risk of developing cancer of the oral cavity is 3 times as great for the heavy smoker and 1½ times as great for the average smoker as for the person who smokes little or not at all.*<sup>33</sup> Conversely, cancer of these sites in the nonsmoking individual is an extreme rarity.

2. **ALCOHOL HISTORY:** Heavy alcohol consumption results in a considerable increase in the risk of cancer of the oral cavity and larynx in the smoker.<sup>33</sup> It is not known whether this holds true for the nonsmoker. The increased risk inherent in heavy alcohol consumption can be summarized as follows: *The risk of de-*

*veloping cancer of the oral cavity is 10 times as great for the heavy drinker (over 6 oz. of whisky or its equivalent per day) as for the average or nondrinker.*

3. **SYPHILIS:** The incidence of carcinoma of the tongue is considerably higher in persons with a history of syphilis. The incidence of positive serologic reaction in patients with this lesion has been as high as 20 per cent in some series.<sup>17</sup>

4. **EXPOSURE TO SUN AND ELEMENTS:** It is well established that the incidence of cancer of the lip and skin of the face is considerably increased among those who by reason of occupation or habit have a history of long term, fairly intense exposure to the sun and elements.<sup>31</sup>

5. **RADIATION THERAPY:** Persons who in the past received indiscriminate and sometimes inept radiation therapy for benign conditions such as acne, hirsutism and similar conditions are particularly prone to develop multiple and recurrent carcinomas of the treated skin after latent periods of several decades.<sup>31</sup> The development of carcinoma of the thyroid following prior radiation of the gland or its environs has also been reported.<sup>9</sup>

6. **SEX:** The selective factors cited thus far apply impartially to males and females, though customarily, by reasons of habit, occupation, etc., they may be found predominantly in men. In the case of thyroid nodules and cancer, however, there is a distinct predilection for women.

7. **AGE:** The incidence of head and neck cancer increases sharply after age 45 in males and age 50 in females.

8. **OCCUPATION:** Skin cancer has been related to occupational exposure to certain substances including soot, tar and petroleum products, arsenic, etc.<sup>31</sup>

9. **BURNS:** There is an increased incidence of cancer in burn scars resulting from thermal, chemical, electrical or other exposures.

10. **OTHERS:** The varied group of *benign oral and dental conditions* producing chronic irritation, as well as nutritional and vitamin deficiencies, are of little assistance as selective aids in cancer detection.

## Methods of Detection

**PHYSICAL EXAMINATION:** Cancer detection methods developed for lesions of these sites fall entirely under the heading of the clinical examination of the particular areas and their lymphatics. No laboratory test has been proposed even as an adjunct to the physical examination. The one which most nearly approaches this is the scintigram, designed to assist in the separation of the suspicious ("cold") solitary thyroid nodule from the innocent ("hot") one. This is not, however, a true screening test since it is applied only to a known nodule. Careful clinical examination emphasizing inspection and palpation, coupled with a heightened awareness of the value of certain selective factors, constitutes the principal method available for detection of cancer of the head and neck.

## LUNG

As used today, the term lung cancer usually denotes bronchogenic carcinoma. Since nearly nine out of ten cases are histologically classified as carcinoma of epidermoid or related tissue types and it is this variety which appears to account for most of the mushrooming increase in incidence of the disease, we shall emphasize this entity.

## The Problem

1956 Incidence: 31,800—  
7.5% of cancer incidence.

1956 Mortality: 29,181—  
12% of cancer mortality.  
19% of male cancer mortality.

Male:female ratio is 6:1.

New York State (exclusive of New York City) reports a 68% increase in male lung cancer mortality over the past 25 years.<sup>10</sup>

## Selective Factors

Abundant epidemiologic evidence is available to identify those persons most likely to develop lung cancer:

1. **SMOKING HISTORY:** Epidermoid lung

cancer is almost exclusively a disease of cigarette smokers. Furthermore, the risk is almost directly proportional to the amount and duration of smoking. The following figures bring this home forcibly.<sup>10</sup> *The risk of developing lung cancer is 60 to 70 times as great for the heavy smoker as for the nonsmoker.* It is estimated that one in eight heavy smokers will develop lung cancer as contrasted to one in 300 in the nonsmoking population.

Discussion of the tobacco-lung cancer problem continues, but we feel that there is no longer room for reasonable doubt. The figures cited speak for themselves.

2. **OCCUPATION:** Persons engaged in occupations which expose them to specific inhalants run a significantly higher risk of developing lung cancer than the general population. Evidence on this score is established with regard to chromates, radioactive ore and asbestos, and suggestive for beryllium, arsenic, nickel and certain petroleum products. The same relationship of intensity and duration of exposure, as with cigarette smoking, applies here. The number of persons sufficiently exposed to these inhalants is relatively small and the importance of this selective factor cannot be compared to the smoking habit.

3. **RESIDENCE:** Lung cancer is considerably more common in cities than in rural areas. This holds true even after allowance is made for the obvious difference in diagnostic and treatment facilities. Careful epidemiologic studies, which have considered all possible environmental factors simultaneously, have demonstrated that most of this urban-rural difference is explained by the difference in smoking habits. There still remains a small difference between the two groups of individuals: the nonsmoker in the city has a slightly higher risk than the nonsmoker in the country. The "urban factor" responsible for this cannot be identified positively but it would appear to be related to air pollution.

4. **AIR POLLUTION:** This selective factor should actually be a part of the residence factor, as noted above. It is listed separately because it has provoked such

widespread interest and publicity in the scientific and lay press. The degree to which so-called air pollution is a cancer hazard appears to vary greatly from city to city, dependent presumably not only upon the intensity of the pollution, but upon the specific substances which may be included in the "smog."

5. **SEX:** Although lung cancer predominates among men by a ratio of between 5 to 9:1, this is primarily a reflection of the difference in the long-term smoking habits of the two sexes.<sup>20</sup> There is every reason to believe that, if present smoking trends continue, the incidence of lung cancer among women will increase sharply in future years and begin to approach the pattern seen among men.

6. **AGE:** The incidence of cancer of the lung increases sharply after age 45 in men and age 55 in women.<sup>6</sup>

## Methods of Detection

1. **PHYSICAL EXAMINATION:** Clinical examination for lung cancer is notably unrewarding in the early case. Except for the stubbornly unresolving or recurring pneumonia secondary to a bronchial neoplasm, or an unusual physical finding which directs attention to the chest, reliance must be placed exclusively on laboratory or technical methods.

### 2. X RAY

a. *Chest fluoroscopy.* Random fluoroscopy by practitioners of varying experience has long been widely used as a routine means of "taking a look at the chest" in the course of a checkup. It has never been proposed by responsible authorities as a means of screening for early lung cancer. It is mentioned here primarily to deplore its misuse for the following cogent reasons: (1) Even under ideal circumstances it is too insensitive to pick up the minute early lesion. (2) It fails to provide a permanent record of findings for future comparative use. (3) It exposes patients unnecessarily to what may be a significant increment in the safely permissible dose of ionizing radiation.

b. *Chest films.* X-ray examination is the most widely used method of screening

for lung cancer. The routine chest film has become a standard feature of hospital admissions, employment examinations and private office checkups. Mass community surveys for tuberculosis have added to the number of adults who periodically have a chest X-ray examination. Mass chest surveys have fallen into disrepute as a means of detecting lung cancer because the high concentration of young adults results in a low cancer yield and the delay in follow-up of suspects is associated with even poorer prognosis.<sup>20</sup> Experience demonstrates, however, that properly read screening films will pick up the vast majority of early lung tumors. Periodic X-ray examinations should be provided for adults over 45, particularly those in the high-risk group.

3. **CYTOLOGY:** Cytologic examination of sputum or bronchial washings by the Papanicolaou technique is now established as a reliable means of diagnosing lung cancer. When three satisfactory deep-cough sputum specimens are provided for examination, 90 per cent of lung cancer can be diagnosed by this relatively simple means.<sup>20</sup> However, inadequate facilities for the cytologic screening of sputum specimens have restricted the utilization of this means of screening for lung cancer. A second limiting factor has been the difficulty of obtaining satisfactory sputum specimens from asymptomatic patients. Recently a major technical advance has been made which should minimize this problem. Using a technique introduced by Barach, Bickerman and Beck, it is possible to obtain adequate, satisfactory sputum specimens from virtually anyone. An aerosol pump nebulizes heated hypertonic saline and propylene glycol. The patient inhales the vaporized solution and soon experiences the urge to cough. The procedure is not unpleasant and the specimens obtained are generally better than those produced spontaneously. The time presently required to obtain each screening specimen (15 to 20 minutes) limits the application of this so-called "sputogenic" machine to the high-risk candidates. It is nonetheless a valuable addition to the field. Further experience will pro-

vide information regarding its sensitivity in the early lesions compared with the chest X-ray examination.

## Summary

Periodic chest X-ray examination of the high-risk adults, identified by evaluation of their smoking, occupational and residence patterns, still remains the principal method available for the detection of lung cancer. To this can be added cytologic examination of the sputum, spontaneous or induced, of selected individuals from within this group. Practical preventive measures may be forthcoming in the future, but this hope does not lessen the need for making more widespread and effective use of the detection methods at hand.

## BREAST

### The Problem

- 1956 Incidence: 45,500—  
10.7% of cancer incidence.  
21.3% of female cancer incidence.
- 1956 Mortality: 22,261—  
9.0% of cancer mortality.  
19.0% of female cancer mortality.

### Selective Factors

Confusion exists regarding the true epidemiologic pattern of breast cancer and, accordingly, it is difficult to list factors which can be used in a practical way to identify the high-risk group for examination. The potentially significant factors exert a less obvious effect than those demonstrated for lung cancer. In detection programs, a factor which increases the cancer risk some 25 per cent above the average is of much less practical value than one whose influence boosts the risk by 6000 per cent.

1. **MARITAL STATUS:** The majority of epidemiologic studies to date indicate that the incidence of breast cancer among single women is higher than among those who are married.<sup>18</sup> This may reflect characteristics predominant in single women, such as the lack of pregnancy or nursing, but this point has not yet been clarified.

2. **NUMBER OF PREGNANCIES:** The risk of developing breast cancer appears to decrease somewhat in proportion to the number of pregnancies.<sup>5</sup>

3. **NURSING:** Many studies have purported to show the protective effect of nursing against the development of breast cancer. There is some evidence that this protection increases in direct proportion to the number and duration of nursing periods.<sup>15</sup>

4. **HEREDITY:** The possible role of hereditary factors has been discussed more with relation to the breast than perhaps any other cancer site. Some maintain that it is an important factor and criticize epidemiologic studies which are negative in this regard on the grounds of superficiality. They maintain that one must search out all the female blood relatives in the cancer patient's genealogy in vertical and horizontal fashion for several generations and obtain accurate pathological information. They believe that this type of study demonstrates family history to be an important factor in breast cancer. Opponents of this theory point out that the occurrence of several cases of this relatively common disease among the female relatives of a breast cancer patient should not be regarded as necessarily significant, particularly if the family is large and the population at risk consequently a sizable one. This controversy has yet to be resolved. In the meantime, it is reasonable to assign those individuals with a strong family history of breast cancer to a potentially high-risk group.

5. **CHRONIC CYSTIC MASTITIS:** Opinion on the importance of this ill-defined clinical entity as precursor to breast cancer is sharply divergent. Some say that its apparent relation to malignant disease is spurious, while others insist that the incidence of breast cancer among patients with chronic cystic mastitis is probably as much as five times greater than the average.<sup>30</sup> Wherever the truth lies, it seems likely that women with this condition will benefit by better medical coverage because of their own heightened breast consciousness and the physician's insecurity in clearly distinguishing between benign

and malignant disease in the presence of chronic mastopathy.

6. **AGE:** The increase in incidence of breast cancer is apparent after age 30.

7. **OTHERS:** *Trauma* has been discussed as a possible etiologic factor in spite of the fact that there is no real evidence that it plays any role in the genesis of the disease. The possible role of *gynecologic aberrations*, such as premature or delayed menarche or menopause, menstrual disturbances, infertility and uterine disease, has been mentioned. These would appear to be attractive possibilities in view of the clear-cut relationship of established breast cancer to hormonal influences, but positive evidence is lacking. *Previous breast disease*, including benign lesions, disorders of lactation, infections, etc., do not appear to play any significant role. *Prior medical treatment*, especially that involving the use of hormones, has been suspected but such a hypothesis still lacks confirmation with regard to the female breast. Finally, it has been demonstrated that the incidence of *diabetes mellitus*, overt or latent, among women with breast cancer is distinctly above average.

### Methods of Detection

1. **CLINICAL EXAMINATION:** Palpation of a lump in the female breast is responsible for the detection or diagnosis of early breast cancer in the vast majority of cases, although occasionally pain, nipple discharge or excoriation may be the first hint of abnormality.

a. *By the physician.* Breast palpation should be accomplished routinely and periodically by the physician in a thorough, systematic fashion.<sup>21</sup>

b. *By the patient—breast self-examination.* Recognizing the fact that about 90 per cent of breast cancers are first discovered by the patient herself, extensive efforts have been made to popularize the practice of breast self-examination. Large groups of women have been indoctrinated by film, brochure and demonstration in the recommended technique. They have been urged to do this at monthly intervals and to consult their family doctors imme-



diately if any abnormality is suspected. A film sponsored by the American Cancer Society has been seen by over 10 million women and several group experiences have been recorded. In general, the reports have been somewhat encouraging; a number of benign and malignant tumors have been detected. However, two drawbacks to this screening method are apparent. First, there is the risk of creating or intensifying cancerophobia. Second, there is a falling-off in the maintenance of the habit. These drawbacks can be minimized if physicians are selective about whom they instruct and if there is a really thorough indoctrination, preferably with some provision for re-emphasis at intervals. The importance of a sympathetic family physician who supports such a program cannot be overemphasized.

2. **CYTOLOGY:** The cytologic examination of breast secretions has not proved useful in screening for cancer because a suitable specimen can be obtained in less than 20 per cent of women, even on provocation by manual expression or a breast pump. It may, however, have diagnostic value when material is available for study. A positive report on a specimen under such circumstances can be helpful, but no reliance can be placed on a negative report.<sup>23</sup>

3. **TRANSILLUMINATION** of the breast is helpful in differentiating solid from cystic masses but is not useful as a general detection technique.

4. **OTHERS:** X-ray or infra-red photography of the breast, as well as the determination of differential skin temperatures or radioactive phosphorus uptake have all had their advocates. None of these techniques has thus far proved suitable for cancer detection, however.

## Summary

A detection program for the control of cancer of this relatively accessible site that provides for routine and periodic breast palpation by the physician and the patient is the most reasonable approach at present. At a future date, it may be possible to establish the significant epi-

demologic leads and formulate the basis for better selection of high-risk groups.

## STOMACH

### The Problem

1956 Incidence: 24,000—  
5.6% of cancer incidence.

1956 Mortality: 22,119—  
9.0% of cancer mortality.

### Selective Factors

In other cancer sites reliance has been placed on epidemiologic or environmental information to pinpoint the high-risk individual for special attention. In cancer of the stomach, however, we must rely largely on medical history and clinical or laboratory tests as avenues of selection.

1. **GASTRIC ACIDITY:** Knowledge of the individual's gastric acidity can be a valuable lead in screening for cancer, since the relationship of the disease to diminished or absent stomach acid has been clearly established. Proof of this is found in the fact that well over 50 per cent of patients with gastric cancer have achlorhydria even after stimulation and still others have diminished acidity.<sup>8</sup> In one prospective study, which followed patients with this condition, the incidence of gastric cancer was estimated to be over five times that expected.<sup>11</sup> Clearly, if means could be provided to measure gastric acidity in large numbers of people, a big step would be taken towards identifying the high-risk population. Several methods have been proposed:

a. **Intubation.** Determination of gastric acidity by this conventional method is quite accurate, but the necessity for passing a tube has sharply limited its widespread application as a screening method.

b. **Tubeless gastric analysis.** This technique was first reported by Segal and his co-workers in 1950 and appears to circumvent most of the obstacles posed by the intubation method.<sup>26</sup> It seems adaptable to large survey work. A resin compound<sup>9</sup> is taken by mouth and, in the presence of measurable gastric acid, an

<sup>9</sup>Obtainable as Diagnex Blue from Squibb & Co.

azure A dye is released and appears in the urine. In most instances, the test is a simple colorimetric one; the appearance of the dye in the urine signifies the presence of acid in the stomach. Some cases require an uncomplicated additional laboratory maneuver to detect the dye in the urine. The procedure is relatively simple, inexpensive and can be carried out at home if the directions are followed carefully. The information provided seems comparable in a qualitative sense to that resulting from intubation.<sup>24</sup> False positive tests are very rare and the occasional false negative appears to be explainable on the basis of inadequate attention to the exact techniques of the test or the tendency of some individuals to secrete acid only intermittently.

c. *Uropepsin*. This test involves determination of the peptic activity of the urine and reflects the known reduction in the secretion of gastric pepsin in stomach cancer. The usefulness of this test is limited to the differential diagnosis of known gastric lesions.<sup>8</sup>

2. **BENIGN GASTRIC DISEASE:** There is a significantly higher incidence of stomach cancer among patients with a well established diagnosis of atrophic gastritis. Individuals with pernicious anemia run five times as great a risk of stomach cancer and they often have changes in their stomach consistent with atrophic gastritis, suggesting a relationship between these entities. A common denominator is diminished or absent gastric acid, a frequent finding in gastric cancer, atrophic gastritis and pernicious anemia. The presence of gastric polyps in an individual should serve to focus attention on the possibility of gastric cancer. An unknown percentage of these polyps are malignant when first detected and many feel that a still larger percentage may undergo malignant change, although there is some dispute on this point. Atrophic gastritis and diminished gastric acidity may coexist with polyps and they in turn may accompany carcinoma. The complex interrelationships among these entities are in need of clarification, but the presence of any of these benign conditions should serve to

place that individual in the potentially high-risk group.

A consideration of the precursor states of stomach cancer would not be complete without mention of gastric ulcer. It is not our intent to deal with the complicated and often frustrating ulcer-cancer problem, especially since most ulcerating lesions of the stomach are symptomatic and worthy of more exacting methods of study than are found in screening programs. The patient with a past or present history of gastric ulcer should be kept under periodic surveillance for possible stomach cancer. Duodenal ulcer is mentioned only because it is important in a negative sense. It is highly unusual for persons with this lesion to develop stomach cancer, the explanation presumably residing, superficially at least, in the high levels of gastric acidity characteristic of this lesion.

3. **BLOOD TYPE:** There is a relatively high percentage of patients with blood type A among those with gastric cancer. The significance of this is not clear and it is not a useful selective factor at present.

4. **HEREDITY:** Several studies have reported a familial tendency in gastric cancer but further evidence is needed before true significance can be assigned to this factor.

5. **AGE:** There is a sharp increase in the incidence of cancer of the stomach in men over 45 and women over 50.<sup>6</sup>

6. **OTHERS:** Good epidemiologic data are lacking with regard to stomach cancer. Efforts to relate it to such factors as tobacco, alcohol, diet, soil composition, occupation, etc., have been unrewarding.

### Methods of Detection

1. **PHYSICAL EXAMINATION** is of no assistance in the detection of early stomach cancer.

2. **X RAY:** X-ray screening programs which have used fluoroscopy, photofluorography, or even routine gastrointestinal series in selected age groups have proved discouraging. They are cumbersome and expensive, prodigal in their consumption of professional and technical

time and low in yield of stomach cancer. The amount of radiation exposure is not a negligible item. X-ray examination, with the prescreening of patients for an acidity, may allow the continued use of this approach in certain groups. Its widespread use, however, does not seem warranted.<sup>8</sup>

3. **CYTOLOGY:** The cytological examination of the gastric contents of asymptomatic individuals cannot be considered a screening device since it requires intubation with consequent discomfort to the patient and is time-consuming. In selected individuals, the cytologic method can be of value in heralding carcinoma before it is detectable by other methods including X-ray examination.<sup>27</sup>

4. **OTHERS:** The utilization of the guaiac test may direct attention to the stomach as the source of bleeding from a malignant lesion. However, the test must be rigidly controlled, with insistence on a prior meat-free diet, and the testing of multiple specimens. If these conditions are fulfilled, the number of "false alarms" will be kept to a minimum. Then, more definitive diagnostic procedures will result in a higher yield of benign and malignant disease of the gastrointestinal tract, including stomach cancer. The electrogastragram has been proposed to compare differences in electrical potential between the gastric mucosa and the skin. Since it involves intubation, its usage seems limited to problems in the differential diagnosis of a lesion. The same can be said of gastroscopy and the recent use of radioactive phosphorus uptake.

## Summary

Periodic X-ray examination of those individuals determined to be at high risk by reason of diminished gastric acidity or known gastric disease is the only method available at present for the detection of stomach cancer. In selected cases, cytologic examination of gastric contents is a valuable adjunct. It is hoped that future epidemiologic studies will provide valuable leads which may assist in the prevention of the disease and in the selection of patients to be screened for its presence.

## UTERUS

Cancer of the uterus consists primarily of two types, epidermoid carcinoma of the cervix and adenocarcinoma of the endometrium. These contrast not only in their basic pathology but also in etiologic and, therefore, selective factors. In considering detection methods, however, they will be dealt with collectively, since the principal detection technique for uterine cancer namely, exfoliative cytology, screens for lesions of both the cervix and endometrium.

### The Problem

1956 Incidence: 38,000—

9.1% of cancer incidence.

17.8% of female cancer incidence.

1956 Mortality: 14,784—

6.0% of cancer mortality.

12.7% of female cancer mortality.

### Selective Factors

The wealth of epidemiologic data regarding selective factors in carcinoma of the cervix stands in sharp contrast to the paucity of data in endometrial or corpus cancer. Accordingly, principal attention will be directed toward those features which are known to characterize the high-risk cervix group.<sup>34</sup>

1. **CIRCUMCISION:** Epidermoid carcinoma of the cervix is more likely to be found among women exposed to uncircumcised sexual partners. Consequently, the disease is relatively uncommon among those racial, religious or national groups in which early male circumcision is the custom. Striking confirmation of this fact is provided by Jewish women, among whom carcinoma of the cervix is 5 to 10 times less common than among their non-Jewish counterparts. This presumably reflects the superior state of penile hygiene of the circumcised Jewish males.

2. **AGE OF FIRST COITUS:** The age at which women first begin regular sexual intercourse has been shown to be an important factor in determining their susceptibility to cervical cancer. The incidence is

higher when regular coitus takes place at an early age. Among virgins and women whose age at first coitus is relatively late, the incidence is correspondingly low. The factors which account for this difference are not clear, but seem to be related to the sensitivity of young cervical tissue and the degree of sexual activity among younger couples.

3. **NUMBER OF PREGNANCIES:** It has been stated frequently that the incidence of cervical carcinoma is related proportionately to the number of pregnancies. This probably reflects the more basic truth that women who marry and begin regular sexual intercourse at an early age are more likely to have large families. The number of pregnancies per se is not the important factor.

4. **PREVIOUS BENIGN GYNECOLOGIC DISEASE:** There is no clear-cut relationship between previous cervicitis, laceration, etc., and increased risk of carcinoma. A history of these conditions is no more frequent among patients with cancer of the cervix than among controls.

5. **AGE:** There is a sharp increase in uterine cancer above age 30<sup>2</sup> and in endometrial cancer, above age 50.

6. **OTHERS:** The apparent relationship between low socio-economic status and increased risk of cancer of the cervix is a specious one, dependent primarily on the early age of first coitus and lack of penile hygiene and male circumcision characteristic of this group. There appears to be no relationship between other medical disease and its treatment (including the use of hormones). Endometrial cancer characteristically occurs in women with a history of menstrual abnormalities, infertility, obesity and diabetes.

### Methods of Detection

1. **PHYSICAL EXAMINATION:** A careful pelvic examination, which includes inspection and bimanual palpation of the uterus and adnexa, is mandatory.

#### 2. CYTOLOGY:

a. *Vaginal and cervical smears.* Cytological examination of vaginal and cervical secretions is the most nearly ideal

cancer detection method yet developed for any body site. It satisfies all the criteria listed in the introductory portion of this article. By virtue of its capacity to detect carcinoma *in situ* and the earliest invasive cancers, cytology can largely prevent death due to cervical carcinoma. Endometrial cancer can also be detected at a much earlier stage and treated with a greater expectation of success. Moreover, the application of cytology to uterine cancer has resulted in a change in our thinking in regard to the natural history of the disease. It should be emphasized that in about two thirds of the cases of pre-invasive carcinoma, the conventional pelvic examination was negative and the diagnosis was made on the basis of cytologic study alone.<sup>14</sup> Some authorities advocate only cervical specimens, while others feel that vaginal sampling is preferable. The latter may be true in community-wide surveys since the vaginal aspiration smear can be taken by a nurse or technician alone without involving physician time. The combination of vaginal and cervical smears is ideal since the vaginal pool is more likely to harbor exfoliated cells from the endometrium. The practice of taking both smears reduces the number of false negatives to a minimum.

b. *Vaginal tampon.* The tampon technique of obtaining vaginal smears was introduced in an effort to broaden the application of cytology and facilitate its use in screening large groups of women.<sup>3</sup> A specially designed tampon is inserted in the vagina either by the patient or physician and allowed to remain in place several hours or overnight. Smears taken from this tampon provide a good sampling of exfoliated cells in the vagina. This technique is useful in case-finding programs where the conventional vaginal and cervical smears are not feasible.

c. *Endometrial aspiration.* The development of a cannula which can be easily and safely introduced into the cervical canal has simplified the problem of adequate sampling of endometrial cells.<sup>15</sup> It is possible that this will lend itself to routine use in detection work although further

(Continued on page 201)

# Progress in Cancer Detection

## II. Cancer Prevention and Detection in the Anus, Rectum and Colon

*This section of the article "Progress in Cancer Detection" has been prepared by Ralph E. Hertz, M.D., and Michael R. Deddish, M.D., Rectum and Colon Service, Memorial Center for Cancer and Allied Diseases, New York, N. Y.*

There have been more than 100,000 detection sigmoidoscopies performed on 35,000 patients at the Strang Cancer Prevention Clinic over an 11-year period. The conclusions and recommendations to be discussed here evolved from this experience as well as from the Rectum and Colon Service at Memorial Center.

### Origin and Distribution of Lesions

Adenocarcinoma constitutes approximately 90 per cent of all cancers in this area. Clinical experience and investigative studies demonstrate that most adenocarcinomas originate in adenomas, which in turn arise in mucosal hyperplasia. The detection and removal of the adenoma is sound cancer prevention. Furthermore, when adenocarcinoma is found and treated in the early stage, a high cure rate is anticipated. Adenocarcinoma has a peak

incidence in the rectum and lower sigmoid, areas accessible to periodic examination. Carcinoid has a similar distribution. The majority of the remaining malignant tumors occur within the perianal skin, perianal structures and anal canal and are also accessible to detection.

### Examination of the Patient

1. **INSPECTION:** Inspection of the perianal skin is an important initial step. Squamous carcinoma and melanoma are the principal lesions found here: True leukoplakia is infrequent, but when seen is to be considered a premalignant lesion.

2. **DIGITAL EXAMINATION:** Rectal digital examination should be carried out by bidigital technique which permits palpation of the perianal tissues between the index finger and thumb. Attention is directed to alterations in the bowel wall, perianal structures and retrorectal space rather than mucosal details, which are better seen than felt. Inflammatory changes and tumors of the perianal soft parts and retrorectal space will be detect-

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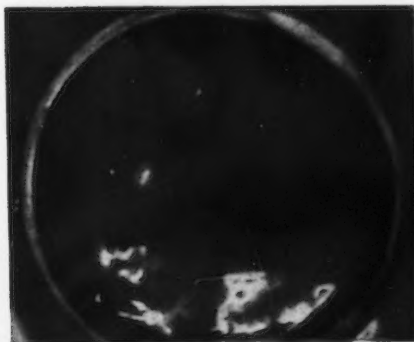


Fig. 1. Hyperplasia—2 mm.



Fig. 2. Hyperplasia with deepening of glands.

ed. Careful palpation of the mucosa of the presacral, or so-called blind area of the rectum, is indicated since occasionally this cannot be visualized. The efficacy of digital examination in the detection of adenomas and adenocarcinomas has been highly overrated in the literature. In a series of 125 carcinomas of the rectum and colon detected, only 13.5 per cent were found by digital examination. *Seven out of eight cancers would have been missed if reliance had been placed on digital examination alone.*

3. PROCTOSIGMOIDOSCOPY is the most important procedure in the examination of the rectum and colon. Approximately 80 per cent of the lesions found were discovered by endoscopy alone. It is relatively simple and safe, but gentleness and thoroughness must be observed. There has been only one bowel perforation in over 100,000 proctosigmoidoscopies at Strang Clinic.

- a. *Preparation for examination.* Proper examination requires a clear lower bowel. A low residue diet should be followed for 24 hours. Two ounces of castor oil is taken at 5 p.m. the day prior to examination, followed by a clear water enema in the morning. This usually results in satisfactory cleansing.
- b. *Equipment.* The ideal sigmoidoscope is a simple 25–30-cm. tube,  $\frac{5}{8}$  in. in diameter, with a good light

and a simple air insufflation unit. Residual secretions are best removed by a strong suction, but, cotton sponges may suffice. If biopsies are performed, a small 3-mm. cup forceps is recommended. The large box forceps is to be avoided.

- c. *Position.* Patients may be examined in the knee-chest or lateral decubitus position, with care to avoid abdominal compression. They should be advised that relaxation is the major factor for an easy examination.
- d. *Technique of sigmoidoscopy.* The sigmoidoscope is introduced slowly in the axis of the anal canal. The obturator is then removed and the instrument is advanced under direct vision. Progression should be gentle, in keeping with the bowel resistance. During introduction, emphasis is placed on passage of the instrument rather than on bowel inspection so that manipulation is minimal and insufflation rarely necessary. Introduction to the full length of the sigmoidoscope should be obtained in 85–90 per cent of cases. The detailed examination is performed while the instrument is being withdrawn in a rotary fashion. Insufflation is used to flatten the folds so that the entire mucosa is clearly seen.

Blood and mucus are sometimes



Fig. 3. Early adenoma—7 mm.

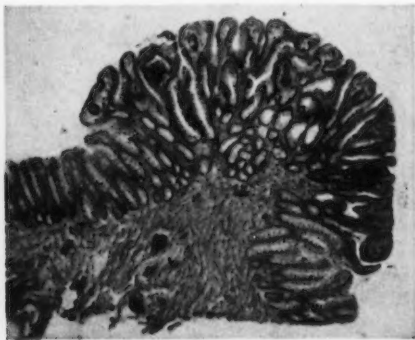


Fig. 4. Adenoma.



seen during introduction, particularly after strong catharsis, within the upper limits of the endoscopic field without a visible bleeding source. These findings indicate the presence of a tumor, diverticulitis or segmental colitis above the level of the sigmoidoscope. A barium enema roentgenogram will usually establish the diagnosis though it will at times be most difficult to rule out co-existing tumors in some cases of diverticulitis. Colonic cytology will often prove of value in detecting neoplasms in these instances.

e. *Management of positive cases.*

Whenever mucosal hyperplasia, adenoma or adenocarcinoma is found, a barium enema with air contrast is performed to rule out the possibility of additional lesions above the sigmoidoscopic field. High-lying colonic adenomas or carcinomas were found in approximately 6 per cent of such cases at the Strang Clinic. If a high-lying polyp is detected radiographically, a confirmatory barium enema is indicated because retained fecal material can mimic a polyp in a solitary study. If the second study is positive, laparotomy and removal of the polyp are advised. In the management of lesions directly visualized through the sigmoidoscope, particular circum-

stances will determine whether biopsy is carried out immediately or deferred until the patient is under therapeutic management. Biopsy should be from the summit of the lesion, as this is the most representative area and least likely to bleed. Lesions of less than 8-10 mm. are not biopsied but left for total removal.

- f. *Follow-up.* A satisfactory detection program for new lesions in these patients consists of an annual sigmoidoscopy and a barium enema with air contrast every other year.

### Summary

A cancer prevention and detection program is for asymptomatic patients and must permit periodic repetition without undue inconvenience or expense. Carefully performed inspection of the perianal area, bidigital rectal examination and proctosigmoidoscopy constitute an adequate routine and should be repeated annually. Barium enema roentgenography and cytologic examination of the colon are added only when indicated by findings or symptoms. The fact that some high-lying lesions will be missed must be accepted within the practical limitations of a detection program.

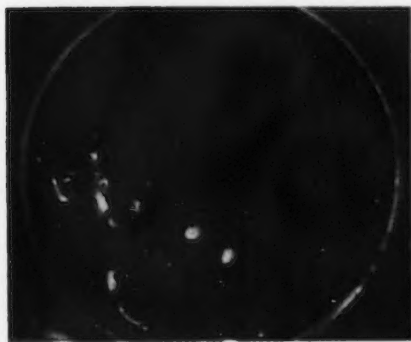


Fig. 5. Large pedunculated adenoma—1 cm.

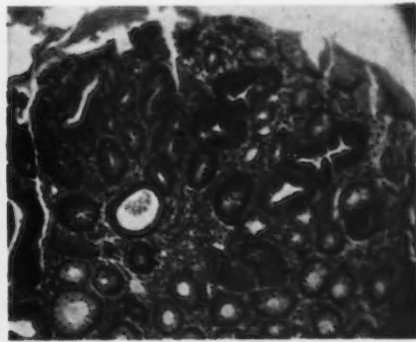


Fig. 6. In-situ carcinoma in an adenoma.

# DISTRIBUTION OF ADENOMAS AND ADENOCARCINOMAS FOUND IN A DETECTION PROGRAM

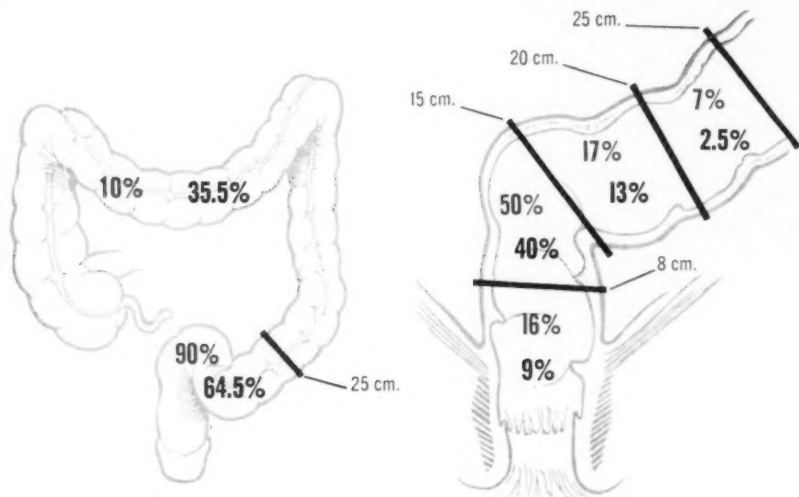
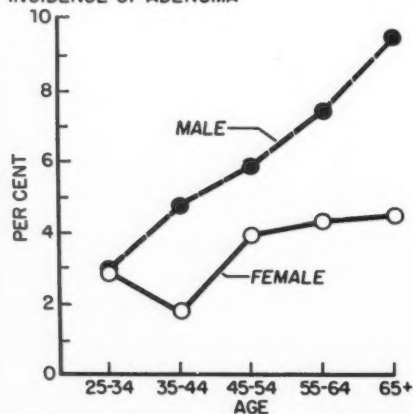
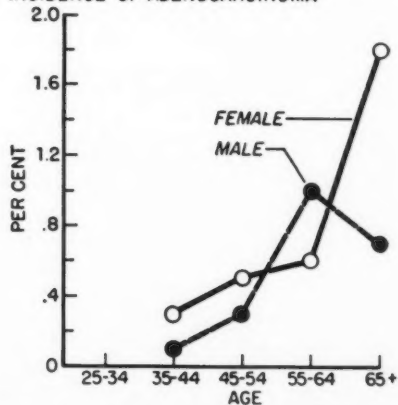


Fig. 7. Percentages of adenocarcinomas shown in black; percentages of adenomas, in red.

## INCIDENCE OF ADENOMA



## INCIDENCE OF ADENOCARCINOMA



The tables on incidence and distribution and the figures that appear in the text do not represent the total Strang Clinic experience to date. They have been derived from analysis of portions of the material and are offered as a guide.

evaluation is necessary. At present its use can be recommended in those instances in which there is suspicion of endometrial disease on the basis of history, clinical examination or vagino-cervical cytology. It is also useful in those cases where conventional cytologic examination may have been inadequate because of cervical stenosis, etc. Endometrial aspiration may yield information which heretofore would have required dilatation and curettement. Certainly at present its employment with appropriate precautions can be recommended.

Realization of the full potential of cytologic methods in detecting cancer of the uterus and other sites has been impeded by lack of trained personnel to screen the slides and separate the normal from the potentially suspicious specimens. It is hoped that the nationwide training program fostered by the American Cancer Society will alleviate this situation. An electronic cytoanalyzer designed to screen submitted slides in large numbers and to decrease the burden imposed on cytology technicians is in process of evaluation. The use of a fluorescent staining technique for initial screening purposes has also been advocated.

3. **IODINE STAIN:** The Schiller test is one of the oldest and simplest of all the cancer detection methods. Nevertheless this practice of painting the cervix with an iodine solution and looking for areas which fail to take the stain still has a place in screening for cervical disease. A positive test reflects the absence of glycogen in certain cervical tissues—a fact which may denote the presence of leukoplakia or carcinoma.

4. **COLPOSCOPY:** This technique has found particular favor among European workers. It amounts to an in-vivo examination of the vaginal and cervical epithelium.<sup>25</sup> The instrument is introduced into the vagina at the time of routine pelvic examination and the tissues are viewed through an optical system which may include magnification. Differential stains applied to the surface under observation provide additional information. Photomicrographs can be made for further evalua-

tion and permanent record. Careful application of this technique may advance knowledge of certain aspects of gynecologic disease. However, it requires expensive equipment, exacting technique and considerable time. From the standpoint of cancer detection colposcopy cannot equal the information provided by vaginal and cervical smears. Its use as a screening method, therefore, is distinctly limited.

5. **OTHERS:** Determination of the electrical potential of cervical tissues as compared with skin surface has been proposed as a method of detecting cervical carcinoma. Subsequent studies have failed to confirm the value of this procedure. Studies involving histochemical and enzyme assays of cervical tissue and estimation of the pH of the vaginal fluid have been reported, but seem far short of practical application as screening techniques at present.

## Summary

In cervical carcinoma and, to a lesser extent, endometrial cancer, the goal of a near ideal cancer detection test appears to have been achieved. Not only that, but practical selective factors are available to identify the higher-risk group where the yield is several fold above the average. In the future, it is hoped that these epidemiologic data can be utilized to introduce practical preventive measures.

## GENITOURINARY TRACT

### The Problem

#### *Cancer of the Male Genital Organs*

1956 Incidence: 28,000—

6.6% of cancer incidence.

13.2% of male cancer incidence.

1956 Mortality: 14,946—

6.0% of cancer mortality.

11.4% of male cancer mortality.

#### *Cancer of the Urinary Tract*

1956 Incidence: 18,500—

4.4% of cancer incidence.

1956 Mortality: 11,717—

4.8% of cancer mortality.

Male:female ratio is 2:1.

## Selective Factors

The urinary bladder is the only genitourinary organ where selective factors are presently applicable. It is true that cancer virtually never affects the circumcised penis, but this is a rare site of cancer in the United States.

1. **SMOKING HISTORY:** Several recent studies have linked smoking, particularly of cigarettes, with an increased incidence of cancer of the bladder. The relationship is not nearly so strong as that between smoking and cancer of the respiratory tract. However, the American Cancer Society prospective study found that the incidence of bladder cancer among regular smokers was approximately twice that expected. This may be the result of some metabolite excreted via the urinary tract.

2. **OCCUPATION:** One of the classical occupational cancers is that affecting the urinary bladder. The high incidence of carcinoma of this organ among certain industrial workers, notably those dealing with aniline dyes, was recognized in the last years of the 19th century.<sup>31</sup> Preventive measures have largely controlled this problem but hazards may appear in new industrial compounds. In these cases the individuals at risk should be periodically surveyed by clinical, laboratory, cytologic and cystoscopic means.

3. **SEX:** This factor is mentioned because of the heavy preponderance of males among cases of bladder cancer, the ratio running as high as 5:1 in some reports. There is no reason to believe that women are inherently less susceptible to bladder cancer and accordingly suspicion has been directed toward an environmental factor peculiar to men, such as long-term smoking, occupation, etc.

4. **AGE:** The incidence of cancer of the prostate increases sharply after age 50; the incidence of urinary tract cancer rises after 45 in males and 50 in females.<sup>9</sup>

## Methods of Detection

1. **PHYSICAL EXAMINATION:** This is virtually the only means by which cancer of the penis and testicle may be detected.

The digital rectal examination is by far the best method of finding cancer of the prostate and abdominal palpation is often the only clue to the existence of renal cancer.<sup>16</sup>

2. **URINALYSIS:** Microscopic examination of the urinary sediment, coupled with a test for occult blood in the urine, should be carried out as part of every cancer detection examination. Gross or microscopic hematuria may denote the presence of carcinoma anywhere in the entire urinary tract. Although there are many benign causes for hematuria, its finding should be the signal for a thorough investigation to rule out the possibility of cancer unless the clinical situation clearly dictates otherwise.

3. **BLOOD TESTS:** The acid phosphatase test for the presence of prostatic cancer is ill-suited to the role of a screening method.<sup>20</sup> Not only is the disease usually advanced before this enzyme is elevated in the blood, but it is well known that even in untreated disseminated disease normal levels are obtained in about 20 to 25 per cent of the cases. More recent efforts to identify and utilize the so-called prostatic fraction of the acid phosphatase enzyme in the blood have not materially changed the situation.

4. **CYTOLOGY:** There was some hope originally that cytologic examination of the urine or prostatic fluid might prove useful in screening for urinary tract cancer. This has not proved to be the case. The low yield of renal and bladder cancer, plus the difficulties inherent in obtaining and preparing proper specimens, have precluded its use for these sites. The same difficulties, plus the unlikelihood of representative exfoliation of malignant cells, have also ruled out its routine use for finding carcinoma of the prostate. Cytologic examination of the urinary sediment can be a useful adjunct once a major suspicion of cancer of the kidney or bladder has been raised. Furthermore, it has a definite role in screening occupational groups exposed to a bladder carcinogen. In this setting it may replace, or at least supplement, periodic cystoscopy as a screening device.<sup>32</sup>

## Summary

It is again obvious that there is need for good epidemiologic information in order that rational selective factors and possible preventive measures may be formulated. Urinary bladder cancer appears to present a fruitful field for research because it is usually of the epidermoid variety, has a strong tendency to be multicentric in origin, recurrent and displays a wide male-female ratio.

The problem of what constitutes clinically significant carcinoma of the prostate still perplexes investigators. Autopsy and surgical studies which show that lesions identical in appearance to full-blown prostatic cancer can be found in 20 to 40 per cent of the asymptomatic adult male population over age 50 raise serious questions about the natural history of the disease and the clinician's responsibility for its detection, diagnosis and management. It is hoped that research will assist in resolving this dilemma and provide practical guideposts in determining the biologic potential of individual lesions.

## RECTUM AND COLON

The conventional division of cancer of the rectum and colon into separate entities is an entirely arbitrary one and difficult to justify on anatomical or physiological grounds. For this reason they are discussed as a single site.

### The Problem

1956 Incidence: 56,000—  
13.1% of cancer incidence.

1956 Mortality: 36,887—  
15.0% of cancer mortality.

### Selective Factors

1. **PRIOR HISTORY OF POLYP OR CANCER:** Any individual who has had one or more benign polyps or cancer of the rectum or colon should be carefully followed and examined with the sigmoidoscope at

regular intervals. The mucosa which has been the site of one such lesion is particularly prone to develop recurrent disease in the same or other areas.

2. **HEREDITY:** This potential selective factor is mentioned because of the known familial predilection of some other polyposoid diseases. Although diffuse polyposis of the colon is a classical example of a genetically determined disease, no hereditary tendency has been demonstrated for simple adenomas of the rectum or colon. This aspect of the problem has not been extensively studied.

3. **ULCERATIVE COLITIS:** The high risk of developing cancer of the large bowel which has previously been the site of ulcerative colitis is well known. Patients with a history of ulcerative colitis must be assiduously followed by means of the sigmoidoscope and, in some instances, by repeated barium enemas.

4. **AGE:** The incidence of cancer of the rectum and colon shows a sharp increase after age 40 for both sexes.<sup>9</sup>

## Methods of Detection

The methods of detecting cancer of the rectum and colon are discussed in detail on pages 197-200.

## THE SKIN

### The Problem

1956 Incidence: 58,000—  
13.6% of cancer incidence.

1956 Mortality: 3715—  
1.6% of cancer mortality.

### Selective Factors

The factors which predispose to skin cancer have been dealt with in the section on Head and Neck. There are no known selective factors applicable to junctional nevi or melanomas. Fair-skinned individuals with a sandy or freckled complexion appear to be more prone to these lesions than the average.

## Methods of Detection

Simple inspection of the patient's skin is the only method available or necessary for the detection of skin cancer. Excision and pathologic examination are customarily advised for all lesions suspicious of basal or squamous (epidermoid) carcinoma as well as those pigmented lesions suggesting junctional nevus or melanoma.<sup>22</sup> Particular attention is paid to nevi situated on the palm of the hand, sole of the foot, in the region of the genitalia or in areas subject to chronic irritation. Increase in size, change in color or a tendency to bleed are obvious indications for immediate removal.

The decision as to which pigmented lesions should be excised is a difficult one. First of all, it is difficult to obtain general agreement as to what constitutes junctional nevi. Clinical descriptions and photographs simply fail to measure up to the task of differentiating, to everyone's satisfaction, the significant lesions from the countless freckles, blemishes, moles, etc., which are encountered in everyday practice. This lack of usable criteria is a major stumbling block to insuring that consistent and proper advice is given to the patient.

Secondly, the true risk of developing a malignant melanoma from a pre-existing junctional nevus is a complete unknown. It is not suspected to be very great in view of the known frequency of nevi and the relative rarity of their malignant analogue. Those who have had experience with this extremely virulent form of cancer may be forgiven if they tend to err on the side of over-caution. However, any program of preventive medicine which too frequently advises surgical measures, often costly and temporarily disabling, runs the risk of defeating its purposes and of discouraging its patients.

A clinical, laboratory or other method is needed which will reduce the number of lesions for which surgery is advised by more precisely identifying the potentially dangerous ones. Estimation of the malignant potential of lesions has been attempted by determining their uptake of radioactive phosphorus, but no practical

clinical application, at least for screening purposes, appears possible at present.

## Summary

Simple inspection of the skin by the examining physician, particularly in susceptible individuals, remains the only method available for the detection of skin carcinoma, melanoma and their precursors.

## LEUKEMIA AND LYMPHOMA

### The Problem

- 1956 Incidence: 29,000—  
6.9% of cancer incidence.
- 1956 Mortality: 22,840—  
9.5% of cancer mortality.
- Male:female ratio is 4:3.

### Selective Factors

1. PREVIOUS RADIATION: Any individual or groups of individuals who have had a history of above-average radiation exposure should be screened carefully and periodically for the presence of leukemia since the relationship between the two entities seems clearly established.<sup>9</sup> There does not appear to be any etiologic relationship between radiation and the lymphomas.

2. EXPOSURE TO TOXIC CHEMICALS: The development of leukemia has been related by some to exposure to chemicals, notably benzene and similar compounds.<sup>31</sup> Individuals whose vocation or avocation places them in contact with these agents should be observed for the possibility of leukemia and related diseases.

3. HEREDITY: No clear-cut familial tendency of the leukemia-lymphoma group has been demonstrated. Proponents of the viral etiology of leukemia and its vertical transmission may challenge this statement. Even if this hypothesis should prove true it is hard to see how it might be utilized as a selective factor in screening programs since these investigators admit to its long and relatively unpredictable latent period and tendency to "skip" generations.



## Methods of Detection

Since leukemia and lymphoma represent a generic grouping and include a number of diseases whose manifestations and pathology may be quite divergent no single detection method will suffice. As we understand these diseases today they are primarily systemic in scope from the very beginning. Certain of the lymphomas may, on occasion, be unicentric in origin with eventual, often very rapid, spread to other regions of the body. The systemic nature of these diseases renders the possibility of cure minimal with present therapeutic agents. Nonetheless, it is important to discover the disease at the earliest possible stage in view of the rare examples of cure and the more frequent instances of long-term survival or palliation.<sup>4</sup>

1. **PHYSICAL EXAMINATION:** Particular attention is paid to the presence of pallor, adenopathy or other abnormal masses, enlargement of the liver or spleen, cutaneous abnormalities, petechiae or bleeding tendencies, etc. Any of these may signal the presence of the leukemia-lymphoma group.

2. **HEMATOLOGY:** Determination of blood hemoglobin, total white-cell count and differential smear of the peripheral blood comprise the usual screening hematologic tests. One or more of these will usually suffice to diagnose, or at least raise suspicion of, leukemia. In addition an abnormal hemoglobin level may suggest the possibility of an occult bleeding neoplasm, especially in the gastrointestinal tract, of a malignant process characterized by bone marrow suppression, or of polycythemia.

3. **CHEST X-RAY EXAMINATION:** The presence of mediastinal widening, hilar adenopathy, pulmonary infiltration, pleural effusions or other abnormality may raise the suspicion of malignant disease, especially the lymphomas.

## Summary

Clinical examination, determination of hemoglobin, total white-cell count and differential smear plus routine chest X-ray

examination are the best methods available for the detection of diseases of the leukemia-lymphoma group. More information is needed regarding the epidemiology of this group to develop better screening methods and selective factors and to explore the even more attractive possibility of preventive measures.

## OTHER SITES

The foregoing sections have dealt with body sites that accounted for 187,200 cancer deaths and 365,400 new cases in 1956. This represents about 75 per cent of cancer mortality and 85 per cent of cancer incidence and is typical of any given year in the United States.

The remaining cancer arises in such sites as the pancreas, ovary, central nervous system, bone, esophagus, small bowel, liver and biliary tracts and soft tissues. It is fortunate that many of these are relatively rare, since they carry a high mortality and do not usually lend themselves to ordinary detection procedures.

## SUMMARY

The foregoing paragraphs have been primarily concerned with the current status of methods of cancer detection and epidemiologic information which can be utilized to define the high-risk group and determine the selection of patients to be examined.

From the standpoint of the private practitioner, the experience in Strang Cancer Prevention Clinic shows that the SUSPICION OF CANCER OF THE ACCESSIBLE SITES IS INITIATED OVER 90 PER CENT OF THE TIME BY METHODS READILY AVAILABLE IN THE PRIVATE OFFICE. These are: (1) Complete history and physical examination including proctosigmoidoscopy. (2) Simple laboratory studies such as hemoglobin, white blood-cell count and differential smear, urinalysis, chest X-ray examination and vagino-cervical smears. This emphasizes the key role which can be played by private physicians in everyday practice.

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## Promises for the Future

The history of cancer chronicled thus far is the history of errors, of illusions, of disappointments, of occasional triumphs. The smile of the Sphinx continues inscrutable.

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It takes a long time to bring excellence to maturity.—Publius

# Progress in Cancer Control through Cancer Registries

*B. Aubrey Schneider, Sc.D.*

For every person in the general population of the United States who has knowledge of at least one cancer cure among his immediate acquaintances, there are four who know cancer only in terms of the death of a close friend or relative. This is one of the findings of a national sample survey of public opinion on cancer conducted by the American Cancer Society in 1956.<sup>6</sup> The prevalence of this fatalistic attitude toward cancer not only conceals the fact that one out of every three cancer patients is now being cured, but also indicates a tendency to emphasize failures and minimize successes insofar as cancer is concerned.

Experience with cancer registries in general hospitals has shown that much of this same tendency to view cancer successes and failures in a ratio that is disproportionate to the true picture exists also among many physicians in general practice. Typically, this attitude arises from the fact that daily practice brings the physician into contact with many more uncured cancer patients than those who have been cured. Then too it should be noted that until an adequate system of follow-up is established in conjunction with a hospital cancer registry there is very little knowledge of the level of salvage actually accomplished in dealing with cancer.

Abundant statistical evidence has now been published to support the conclusion that over-all cancer survival rates, as well as those for certain major sites of cancer, have improved over the past 10 to 15 years.<sup>4, 5</sup> The effectiveness of cancer control is best measured by the end results (survival rates) attained. However, such results can be brought to light only through careful compilation of adequate

clinical records covering the diagnosis, treatment and follow-up of patients with the disease.

In an effort to stimulate progress in the inauguration and maintenance of adequate cancer patient records, the American College of Surgeons, since January 1, 1956, requires as an essential feature for its approval of a hospital cancer program, the establishment of a cancer registry.<sup>1</sup> Such a registry consists of a working file of abstracts covering the pertinent information on the diagnosis, treatment and follow-up of every patient with a discharge diagnosis of cancer. It thus provides the necessary raw data for the assessment of the total cancer problem in the institution. The cancer registry has been defined as a tool for measuring the quantity and quality of medical care for cancer patients. In the two and a half years since the inauguration of the registry program by the American College of Surgeons, the hospital cancer registry has proven itself to be not only an effective mechanism for the measurement of progress in cancer control, but also a potent factor in the stimulation of that progress. It is the purpose of this paper to examine several of the elements of a registry program, particularly from the standpoint of the stimulus they are providing to the current trend of progress in cancer control.

Basic to this discussion is a definition of cancer control which embraces all of those factors which are related either directly or indirectly to the quantity and quality of medical care for the cancer patient. This definition includes the level of physician and patient interest, quality of diagnosis and therapy, adequacy of follow-up and even basic record keeping. Improvement in any of these areas is indicative of progress in cancer control, and it is precisely in these areas that the cancer

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registry program has its greatest potentiality in stimulating progress, particularly in the small to moderate size general hospital.

In a general hospital of 150 to 200 beds it is obvious that the cancer records would have to be accumulated for many years before they would yield material for any substantial quantitative significance. This is one of the reasons for the current popularity in some areas of the country of the so-called central registry in which the cancer records from a group of small hospitals are pooled for the purpose of studying cancer care at the community or county level. There is evidence that the quantity and quality of medical care for cancer patients in the small general hospitals is something less than that provided by the specialized cancer hospitals and clinics or the larger teaching centers. For example, in Connecticut, the proportion of microscopically confirmed cases from 1947 to 1951 was 89 per cent in hospitals with more than 300 beds, and 82 per cent for hospitals with less than 150 beds.<sup>4</sup> Similarly, Bleicher, using cancer of the colon and rectum as an example, has noted that the rate of curative resection is lower; the operative mortality rate is higher; follow-up is less complete; and the survival rate is lower for cancer patients treated in the general hospital than in the larger medical centers. Bleicher concludes that "Ewing's criticism of the unsatisfactory treatment of cancer in the average general hospital is as valid today [1949] as it was twenty years ago."

The proportion of all cancer patients in the United States diagnosed and treated in the small general hospital is difficult to estimate. Bleicher believes that the "vast majority" are treated in such facilities; a viewpoint which is probably better understood when it is realized that his report, which is intended to demonstrate the situation in the "small hospital," is based on the experience of a "midwestern hospital of 500 beds in a city of 150,000 population." In Connecticut where the central registry has collected cancer records from hospitals representing 94 per cent of the general hospital beds in the state, nearly

half of the records have come from hospitals with less than 300 beds.<sup>4</sup> General hospitals of less than 300 beds represent 75 per cent of all the hospitals in Connecticut.<sup>7</sup> In the nation as a whole general hospitals of less than 300 beds account for 90 per cent of the total of such institutions; they represent nearly 60 per cent of all available general hospital beds; and what is more to the point here, they cover 70 per cent of all general hospital admissions.<sup>7</sup> From this it is apparent that a conservative estimate would place at least 50 per cent of all cancer admissions in the United States in general hospitals of less than 300 beds.

Since a large proportion of cancer patients receive their first definitive diagnosis and therapy in the small general hospital, and because the level of accomplishment in dealing with the disease is considerably lower in this type of institution than in the larger medical centers, it is apparent that the greatest need for improvement in the quantity and quality of medical care for cancer patients is in the small community general hospital. It is in this type of institution that the cancer registry has its greatest potential value in terms of progress in cancer control.

Because of the very nature of the problem, there is still little published evidence in support of this general conclusion, hence, the following observations of the author in his role as consultant in the development of cancer registry programs throughout the United States over the past 10 years.

One of the first "by-products" of a hospital cancer registry is the improvement of hospital records. This was demonstrated recently in a rather dramatic fashion when a small hospital made a preliminary analysis of the first few hundred cancer records accessioned in its registry. The analysis shows that 65 of the first 67 registered cases of carcinoma of the liver were designated as primary. This appeared to be such a startling finding that the hospital cancer committee—physicians interested in cancer—reviewed the charts in question. They were rather surprised to find that in only a very few cases was

there any notation in the chart as to whether the tumor was primary or metastatic. Further, they found that the ground rules, which they had developed for the guidance of their registrar—a medical secretary—in abstracting the charts, stated that when there was no notation on the chart as to whether the tumor was primary or metastatic, she was to “assume that it was primary.” In this fashion a basic lesson was learned; namely, that statistical analysis cannot improve the quality of information drawn from the original charts; it merely demonstrates it.

Similarly, another preliminary analysis of the cancer records in a small hospital revealed that in more than a third of the registered cases, the stage of the disease at diagnosis was unspecified. The hospital cancer committee reviewed some of the original hospital charts of these cases and confirmed the finding. Further, as they reviewed the charts, they recognized some of the cases as their own patients, and knew the stage at diagnosis. Strangely enough, it was largely the cases with localized disease (stage I) for whom the physicians had neglected to make the necessary notation on the original chart. The fact that improvement in record keeping can bring an apparent increase in the proportion of cases with localized disease has been substantiated by later analyses which have shown that as the proportion of “stage unspecified” cases has decreased over the years, the per cent of stage I cases has increased with relatively little change occurring in the proportions of stage II and stage III cases, i.e., cases with regional extension or metastases, and cases with remote or generalized metastases, respectively.

When these and similar discrepancies in the hospital records of cancer patients are brought to the attention of the physicians at staff meetings, seminars, etc., their interest and cooperation is usually stimulated to the point where they react by improving the charts of the cancer patients. Hubly has commented as follows concerning the function of a small (county) registry: “One effect of the registry has been that of greatly improving

the keeping of hospital records as they relate to cancer. This improvement has been brought about through greater interest among the attending physicians, residents and interns. For example, records are now signed out with more attention paid to the specificity of primary site and extent of disease, and as to whether the treatment was definitive or palliative, and finally, with a statement as to whether the patient is free or not free of cancer when he leaves the hospital.” Although the matter of record keeping may appear to be only indirectly related to the cancer problem, any improvement in this area, stemming from increased physician interest, may be considered as progress in cancer control. Such progress is in evidence in many small general hospitals as a result of the establishment of a cancer registry program.

Progress in cancer control, by way of increased physician interest, is being stimulated in a more direct way by several additional elements of a hospital cancer registry program. For example, the general principle that microscopic confirmation of a malignant tumor accrues to the benefit of both the physician and the patient in the management of the disease is so universally taught and accepted that every hospital staff to which the question has been put has felt that the percentage of microscopically confirmed cases in their institutions must be close to 100. However, except in those rare instances in which only microscopically confirmed cases are registered (in which case the remainder of the cancer problem in these institutions is largely forgotten!), the closer look usually reveals a level of diagnosis of the order of 60 to 65 per cent. To the staff this is usually a startling revelation; and they become aware, sometimes for the first time, of the number of records with discharge diagnoses of “probable” or “possible” cancer, or cancer based on X-ray or other clinical evidence only. Such a finding is inevitably followed by an increase in the proportion of microscopically confirmed cases; in one small registry the proportion of such cases increased from 60 per cent to 85 per cent over

a subsequent period of seven years.<sup>9</sup>

Similarly, the most elementary compilation of survival figures from a small hospital or a group of hospitals is usually very enlightening to the local medical group. In studying the salvage rates for cancer by site in their hospital, a group of physicians learned that of the total 42 cases of cancer of a particular site which they had treated during a five-year period, not one case survived more than three years. At a monthly staff meeting a lively discussion ensued. From the discussion the conclusion was reached that the poor salvage for these cases was due entirely to lack of training and interest on the part of the surgeons who were attempting to handle them. Whereupon they took the necessary steps to bring a specialist newly trained in that cancer site into their community to deal with this problem as part of a general surgical practice.

Even the difficult task of follow-up is capable of stimulating physician interest in the cancer problem. In the maintenance of a system of follow-up for cancer patients, the registry establishes contact with all the physicians in the community responsible for referral, treatment or care of cancer patients, encouraging them to provide follow-up information periodically on all such patients. In the establishment of such a follow-up scheme in a small hospital recently many of the physicians were pleasantly surprised to learn that some of their patients with whom they had lost immediate contact and a few of whom

they had entirely forgotten were still alive and well as long as eight years following diagnosis and therapy. This simple bit of information had a most salutary influence in stimulating physician interest in the cancer problem in this hospital.

In summarizing the over-all effect of the cancer registry program in terms of physicians' interest, Hubly has made the following statement: "The registry has been an effective agent for professional education in bringing the problems of cancer at a community level to the attention of the practicing physician. It has made the physician aware of the areas in which the diagnosis, treatment and care of cancer can be improved. It has stimulated physician interest in cancer control. The pooling of records in a central registry makes possible the impartial study of cancer as it exists and as it is being handled throughout the county. Although the volume of material thus far accumulated by the central cancer registry is not quantitatively spectacular, it is of such a quality as to indicate the value and importance of concentrated and cooperative effort in dealing with the problem of cancer control."

To this can be added only a final statement that the cancer registry program throughout the United States is becoming an increasingly effective force in stimulating progress in cancer control; and further, that its impact is greatest in the place where it is needed most; namely, in the small general hospital.

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hope of cure by radical mastectomy and actually may be harmed by surgical spreading of the disease. Inoperable patients are best treated by radiation -- higher voltage is better than conventional.

Kholdin (Leningrad): "Complex therapy" has yielded five-year survival rates of 85 per cent of stage I, 35 per cent of stage II and 27 per cent of stage III breast cancer cases in 3000 patients treated. Treatment consists of complete or partial radical mastectomy with pre- or post-operative radiation of areas of potential spread. For far-advanced breast cancer radiation plus hormones (testosterone or progesterone) are indicated. Complex treatment includes general tonics and careful, repeated examinations of blood, endocrine and nervous systems.

Baclesse (Paris): Irradiation alone of breast and axillary subclavicular and internal mammary nodes has yielded these five-year cure percentages: Stage II, 55; stage II-plus, 23.8; stage III, 16.6; stage III-plus, 21.7.

Doll (London): Irradiation causes acute, monocytic or chronic myeloid leukemia in man, but it is uncertain whether it can cause chronic lymphatic leukemia.

Johansen (Copenhagen): Relatively large doses of thorium, hypodermically, induced animal sarcomas; intravenously, it caused disseminated reticuloendotheliosarcoma, mainly in spleen, liver and lungs, where it was deposited. Tumors appeared from one to several years after administration. Among 250 human beings who were contaminated with (10-80 ml.) thorotrast 10 to 20 years ago, there is as yet no increased cancer rate, although the literature shows 10 human cases resembling those produced by thorium in animals.

Blokhin (Moscow): Different drugs (novoembichin, dopan, sarcolysin, omain) produce different effects on different tumors. The search for a universal anticancer drug is futile. Experimental work should be carried on along lines of differentiated treatment for tumors.

Bichel (Aarhus, Denmark): Diepoxytutane (dl-form) has yielded promising results against Hodgkin's disease.

Heilmeyer (Freiburg, Germany): Hodgkin's disease cases treated by radiation alone survived 29.8 months and by a combination of radiation and cytostatic agents, 56.5 months. Women lasted longer than men (66.7 against 49.4 months).

Emmelot (Amsterdam): The fatty acid oxidation

cycle, not the citric acid cycle, in Ehrlich ascites cells is inhibited in the presence of glucose. Styrylquinolines inhibited DPN-linked oxidation and activated liver mitochondrial ATPases and ascites cell aerobic and anaerobic glycolyses.

Boulanger and Osteux (Lille): D-alanine is yielded by cancer tissue incubated in the presence of dl-alanine.

Polli (Milan): DNA from normal, lymphatic and myeloid leukemic cells have different sedimentation rates.

Quastel (Montreal): Sarcomycin inhibits amino acid incorporation into Ehrlich ascites cell protein in proportion to its inhibition of  $P^{32}$  turnover in ATP. It is less effective on embryonic and adult tissues and has no effect on yeast.

Kit et al. (Houston): Glucose depressed and glucose plus methylene blue stimulated respiration in several tumors tested. DNA content and oxygen uptake of cells were related to the chromosome numbers.

Hultin (Stockholm): Reactive liver carcinogens may act as cytoplasmic mutagens. Aminofluorene bound strongly to microsome particles incubated in the presence of TPNH or a TPNH-generating system -- and did not bind in their absence. DPNH could substitute for TPNH only to a limited extent. Binding was inhibited by sulphydryl reagents, cysteine, glutathione or strong chelates.

Zamecnik et al. (Boston): A free amino acid in its incorporation into protein sequentially (1) reacts with ATP, (2) attaches to soluble RNA by a linkage as yet unknown and (3) takes its place in peptides in microsomal RNP. Terminal mononucleotides (ATP, CTP, UTP) are incorporated into the RNA via phosphorylytic cleavage of triphosphates. Normal rat liver and cancerous mouse ascites tumor cells probably use the same pathways, although the tumor cells have less ATPase.

Green (Leeds): The evidence indicates that chemical carcinogens become antigenic on binding with tissue protein, that tumors produce antibodies against host tissues, that antigenic lipid complexes (lipoproteins and phospholipids) may be released from tumors as a result of immune reactions in and around the tumors and that the cancer state results from a cytoplasmic deficiency of a lipoprotein complex. Lack of tissue-specific antigens could account for the anaplasia, increased growth rate, invasion, metastasis and aggression of cancer.

## COMING MEDICAL MEETINGS

<b>Date 1959</b>	<b>Meeting</b>	<b>City</b>
Jan. 22-24	Cancer Seminar, Arizona Division, American Cancer Society, Inc.	Tucson
Jan. 27-29	Cancer Seminar, Alabama Division, American Cancer Society, Inc.	Birmingham
Feb. 6-7	American College of Radiology	Chicago
Feb. 10-13	Mid-South Post Graduates Medical Assembly	Memphis
Feb. 22-25	California Medical Association	San Francisco
Feb. 26-28	M.D. Anderson Hospital and Tumor Institute Symposium on Fundamental Cancer Research: Genetics and Neoplastic Growth	Houston
Mar. 8-9	American Broncho-Esophagological Association	Hot Springs, Va.
Mar. 8-9	American Laryngological Association	Hot Springs, Va.
Mar. 10-12	American Laryngological, Rhinological and Otolological Society	Hot Springs, Va.
Mar. 17-19	National Health Council	Chicago
Mar. 19-21	Alaska Territorial Medical Association	Juneau
April 1-3	American Association of Anatomists	Seattle
April 5-9	American College of Obstetricians & Gynecologists	Atlantic City
April 6-8	American Radium Society	Hot Springs, Va.
April 6-9	American Academy of General Practice	San Francisco
April 10-12	American Association for Cancer Research	Atlantic City
April 12-16	American Physiological Society	Atlantic City

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